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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/018,170	12/11/2001	Henry Yue	PF-0733 USN	8478

27904 7590 04/20/2004

INCYTE CORPORATION
3160 PORTER DRIVE
PALO ALTO, CA 94304

EXAMINER	
STEADMAN, DAVID J	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 04/20/2004

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 03312004

Application Number: 10/018,170
Filing Date: December 11, 2001
Appellant(s): YUE ET AL.

James M. Verna
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed January 30, 2004.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

The rejection of claims 205-206, 208-209, 211-215, 217, 224-226, and 228-231 under 35 USC § 101 stand or fall together because appellant's brief does not include a statement that this grouping of claims does not stand or fall together and reasons in support thereof. See 37 CFR 1.192(c)(7).

The rejection of claims 205-206, 208-209, 211-215, 217, 224-226, and 228-231 under 35 USC § 112, first paragraph, stand or fall together because appellant's brief

does not include a statement that this grouping of claims does not stand or fall together and reasons in support thereof. See 37 CFR 1.192(c)(7).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

Morgan et al. (1998) FEBS Lett 434:300-304

Brenner et al. (1998) PNAS 95:6073-6078

Shattuck-Eidens et al., 1997, US Patent 5,693,473

Murzin et al. (1995) J Mol Biol 247:536-540

Brenner (1999) Trends Genet 15:132-133

Brown et al., 1998, US Patent 5,807,522

Rockett et al. (1999) Xenobiotica 29:655

Lashkari et al. (1997) PNAS 94:8945

Nuwaysir et al. (1999) Mol Carcinogen 153:24

Steiner et al. (2000) Toxicol Lett 467:112-113

Gerke et al. (2002) Physiol Rev 82 :331-371

Lecona et al. (2003) Biochem J 373:437-449

Lecat et al. (2000) J Cell Sci 113:2607-2618

Nguyen et al. (2000) J Biol Chem 275:29466-29476

Blankenberg et al. (2000) Eur J Nucl Med 27:359-367

Rockett et al. (1999) Environ Health Perspectives 107:681

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Rejection under 35 USC § 101

Claims 205-206, 208-209, 211-215, 217, 224-226, and 228-231 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

The claims are drawn to the polynucleotide of SEQ ID NO:64, the encoded polypeptide of SEQ ID NO:12, an array or microarray comprising said polynucleotide, methods of making and using the polypeptide of SEQ ID NO:12, and methods of using said microarray.

The specification discloses that the nucleic acid of SEQ ID NO:64 encodes the polypeptide of SEQ ID NO:12 (see page 73 of the specification). Page 80 of the specification further discloses that the amino acid sequence of SEQ ID NO:12 is "homologous" to the amino acid sequence of annexin 31 as disclosed by Morgan et al. (FEBS Lett 434:300-304; cited in the Office action mailed January 10, 2003). The specification asserts the claimed invention is useful "in the diagnosis, treatment, and prevention of cell proliferative, autoimmune/inflammatory, neurological, gastrointestinal, reproductive, and developmental disorders" (page 1, lines 5-7 and page 7, lines 13-15). The specification further asserts the claimed invention is useful, inter alia, for protein expression (page 31), as an antigen for producing antibodies (page 41), or for monitoring gene expression (pages 55-56). The claimed invention does not meet the utility requirement of 35 USC § 101 because the specification fails to assert a specific

and substantial utility or to disclose a well-established utility for the claimed polynucleotide, polypeptide, and array.

Regarding the asserted utilities of diagnosis, treatment, and prevention of cell proliferative, autoimmune/inflammatory, neurological, gastrointestinal, reproductive, and developmental disorders, it is noted that the specification fails to disclose a correlation between the claimed polynucleotide and/or polypeptide and a specific cell proliferative, autoimmune/inflammatory, neurological, gastrointestinal, reproductive, and developmental disorders. Instead, the specification discloses a vast number of cell proliferative, autoimmune/inflammatory, neurological, gastrointestinal, reproductive, and developmental disorders (see, e.g., pages 52-53) that "may" be diagnosed, treated, and/or prevented using the claimed compounds without providing any specific guidance as to which of those disclosed diseases – if any – can be diagnosed, treated, and/or prevented using the claimed compounds. Even if the specification identified specific cell proliferative, autoimmune/inflammatory, neurological, gastrointestinal, reproductive, and developmental disorders that can be diagnosed, treated, and/or prevented using the claimed compounds, the specification fails to provide the guidance necessary for diagnosing, treating, and/or preventing any particular disorder, particularly those that are considered to be cell proliferative, autoimmune/inflammatory, neurological, gastrointestinal, reproductive, and developmental disorders. MPEP 2107.01 defines a "substantial utility" as a utility that "defines a 'real world' use" and that "[u]tilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities." In this case, further

experimentation is required to use the claimed polynucleotide, polypeptide, and array for diagnosing, treating, and/or preventing a cell proliferative, autoimmune/inflammatory, neurological, gastrointestinal, reproductive, and developmental disorder. Therefore, this type of utility is not considered a "substantial utility". See Brenner v Manson, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966).

Regarding the asserted utilities of protein expression, for producing antibodies, and monitoring gene expression, it is noted that any polynucleotide can be used for protein expression, any polypeptide can be used as an antigen, and any polynucleotide can be used as a component of an array for expression analysis. MPEP 2107.01 defines a "specific utility" as a utility that "is specific to the subject matter claimed", which "contrasts with a general utility that would be applicable to the broad class of the invention." As the asserted utilities of protein expression, antigen for producing antibodies, and monitoring gene expression apply to the broad class of polynucleotides and polypeptides, none of these utilities is specific to the claimed invention.

Moreover, regarding the use of the claimed compounds and array for expression analysis, MPEP 2107.01, describing utilities that are not substantial, states, "[a] method of assaying for or identifying a material that itself has no specific and/or substantial utility." In this case the use of the claimed compounds and array for expression analysis is a use that involves assaying for a material, i.e., the claimed compounds, that have no specific and substantial utility. Furthermore, the use of the claimed compounds and array for expression analysis would require further research to identify a "real world" use

as the specification fails to provide guidance for interpreting the results obtained thereby.

Rejection under 35 USC § 112, First Paragraph

Claims 205-206, 208-209, 211-215, 217, 224-226, and 228-231 are rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a substantial or specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

(11) Response to Argument

Rejection under 35 USC § 101

Appellants traverse the instant rejection by arguing that the claimed polynucleotide and polypeptide have use in toxicology testing, drug development, and the diagnosis of disease, without requiring knowledge of the function of the encoded polypeptide.

It is the examiner's position that, because the specification fails to provide the guidance necessary for a skilled artisan to use the claimed invention for these asserted utilities, further research is required to identify or reasonably confirm a "real world" context of use for the claimed invention as explained in greater detail below. The examiner acknowledges that the utility requirement does not require knowledge of

biological function of a claimed polypeptide and/or polynucleotide to satisfy the utility requirement of 35 USC § 101. This point is also explained in greater detail below.

Appellants argue the similarity of the claimed polypeptide to another polypeptide of known, undisputed utility demonstrates utility beyond the reasonable probability required by law. Appellants argue that INTRA-12 (SEQ ID NO:12) shares 98% sequence identity with annexin 31, which is more than enough homology to demonstrate a reasonable probability that the utility of annexin 31 can be imputed to the claimed invention. Appellants argue that given the homology of SEQ ID NO:12 to annexin 31, the probability that the claimed polypeptide is related to annexin 31 is very high (citing Brenner et al. PNAS 95:6073-6078 in support of their argument). Appellants argue the "fact" that the claimed polypeptide is a member of the annexin family alone demonstrates utility as each member of this class is allegedly useful, regardless of its function. Appellants argue that because there is no evidence that any member of this class of polypeptides would not have some patentable utility, it follows that there is a substantial likelihood that the claimed polypeptide also has patentable utility, regardless of function and that the law allegedly has never required a patentee to prove more. Appellants' argument is not found persuasive.

There is no dispute that the sequences of SEQ ID NO:12 and human annexin 31 as disclosed by Morgan et al. (supra) share a high level of amino acid sequence identity. However, this relationship between the sequences does not confer patentable utility on the claimed invention. While the utility of the annexin class of polypeptides is not at issue, even if SEQ ID NO:12 was classified as an annexin, it should be noted that

there is no evidence of record to indicate that all members of this "class" of polypeptides have patentable utility. As late as 1998, Morgan et al. (supra) attest to the lack of understanding of the biological significance of annexins, by teaching, "[t]he biological function(s) and phenotypic profile(s) of annexins remain unsolved" (page 300, left column, top). Moreover, Morgan et al. (supra) teach that annexin 31 is an unconventional annexin, having a distinct expression pattern, an amino acid sequence that is atypical of annexin family members, and has no calcium binding sites (page 303, Discussion). Thus, it is not clear from the prior art that either all annexins (or specifically annexin 31) have any specific utility that can be imputed to the claimed polynucleotide or polypeptide. While the homology between the sequence of SEQ ID NO:12 and annexin 31 is sufficient to believe that they may have the same utility, it is not clear what utility both proteins have.

Appellants argue evidence of "direct proof" of the utility of the claimed invention is provided by the Declarations of Bedilion and Furness, allegedly describing uses of the claimed invention in gene and protein expression monitoring. Addressing the Bedilion Declaration, appellants assert Bedilion describes how the claimed polynucleotide can be used in gene expression monitoring applications, and how those applications are useful in developing drugs and monitoring their activity. Appellants quote from the Bedilion Declaration, which states (in summary) that a cDNA microarray containing a SEQ ID NO:12-encoding polynucleotide would be a more useful tool than a cDNA microarray lacking same in connection with conducting gene expression monitoring studies on proposed or actual drugs for treating cancer, immune disorders, neurological

disorders, and gastrointestinal disorders for such purposes as evaluating their efficacy and toxicity. Appellants argue the examiner does not dispute the use of the claimed polynucleotide as a probe in microarray expression analysis and that the examiner contends the claimed sequence cannot be useful without knowledge of its biological function, which is not required by law to prove utility. Appellants argue that, as demonstrated by the Bedilion Declaration, beneficial results can be achieved from the claimed polynucleotide in the absence of any knowledge of the function of the encoded protein and assert that the use of the claimed polynucleotide in gene expression monitoring applications is independent of its function.

It is noted that Dr. Tod Bedilion is a consultant for Incyte Corporation and thus is a concerned party. Regarding the merit of the examiner's position, any polynucleotide can be used in a microarray. This asserted utility is not specific to the claimed invention. In this case, the specification fails to provide evidence that SEQ ID NO:64 or the polypeptide encoded thereby is a target for drug development, toxicology studies, or disease diagnosis. Furthermore, the specification fails to provide guidance for using the claimed compounds for drug development, toxicology studies, or disease diagnosis by expression analysis, e.g., how a skilled artisan would use data relating to the claimed polynucleotide derived from the results of gene expression analysis and what the results would mean. As such, additional research is required to identify a "real-world" context of use for the claimed compounds. There is no dispute that the claimed polynucleotide can be used as a probe, however, this utility is not specific to the claimed polynucleotide. As one of ordinary skill in the art would recognize, any nucleic acid can be used as a probe

– this utility is not specific to the claimed nucleic acid and instead applies to the broad class of nucleic acids. Contrary to appellants' assertions, the examiner acknowledges and agrees that the utility requirement does not necessarily require knowledge of biological function as long as there is a specific, substantial, and credible asserted utility or a well-established utility for the claimed polynucleotide. For example, contrast the claimed invention, which has no specific and substantial asserted utility, with Shattuck-Eidens et al. (US Patent 5,693,473), who teach mutant alleles of the *BRCA1* gene that predispose a patient to developing breast and ovarian cancers (abstract). While there is no disclosure of the function of the mutant *BRCA1* genes or their gene products, the invention nevertheless has utility as being an indicator for susceptibility to developing breast and ovarian cancers.

Appellants argue that in view of the Furness Declaration, a skilled artisan would have understood the uses of the claimed polypeptide in protein expression monitoring techniques such as 2-D PAGE and western blots, for assessing the potential toxic effect of a drug candidate. Appellants argue the examiner does not dispute the use of SEQ ID NO:12 in 2-D PAGE gels and western blots in drug toxicity monitoring and that the examiner contends that the polypeptide cannot be useful without knowledge of its function, which is not required by law to prove utility. Appellants' argument is not found persuasive.

The examiner agrees with appellants' arguments to the extent that, along with any other protein, SEQ ID NO:12 can be used in 2-D PAGE gels and western blots in drug toxicity monitoring – this non-specific use applies to the broad class of proteins.

Furthermore, the specification provides no guidance to allow a skilled artisan to use data relating to the claimed polypeptide derived from the results of toxicity testing and what the results would mean. For example, if the expression of the claimed polypeptide were monitored in a drug toxicity test, the specification provides no basis on which a skilled worker would be able to determine whether that result is meaningful. As such, further experimentation would be required to interpret the results of such expression analysis. Also, as stated above, the examiner acknowledges that the utility requirement does not necessarily require knowledge of polypeptide biological function. A claimed polypeptide can meet the requirements of utility as long as the specification discloses a credible, specific and substantial asserted utility or a well-established utility for the claimed polypeptide, even though the function of the polypeptide is not disclosed in the specification.

Appellants cite the following case law as allegedly being relevant to the instant rejection: Anderson v Natta, 480 F.2d 1392, 1397, 178 USPQ 458 (CCPA 1973); Brenner v Manson, 383 US 519, 534-35, 148 USPQ 689 (1966); Juicy Whip Inc. v Orange Bang Inc., 51 USPQ2d 1700 (Fed Cir 1999); Stiftung v Renishaw PLC, 945 F2d 1173, 1180, 20 USPQ2d 1094 (Fed Cir 1991); Standard Oil Co. v Montedison, S.p.a., 212 USPQ 327 343 (3d Cir 1981); Cross v Izuka, 753 F2d 1040, 1048 (Fed Cir 1985); Nelson v Bowler, 626 F2d 853, 856, 206 USPQ 881 (CCPA 1980); In re Cortright, 165 F3d 1353, 1357, 49 USPQ2d 1464 (Fed Cir 1999); In re Brana, 51 F3d 1560, 1566; 34 USPQ2d 1436 (Fed Cir 1995); and In re Langer, 503 F2d 1380, 1391-92, 183 USPQ 288 (CCPA 1974). The essential disagreement between the examiner's position and

appellants' position appears to be the interpretation of what constitutes a specific and substantial asserted utility, as will be explained in detail below.

Appellants argue the claimed invention meets all necessary requirements for establishing a credible utility under the law as appellants allege there are "well-established" uses for the claimed invention, and there are allegedly specific practical and beneficial uses disclosed in the specification for the claimed invention. Appellants argue these uses are explained in the Bedilion and Furness Declarations and that objective evidence, allegedly not considered by the Office, further corroborates the credibility of the asserted utilities. Appellants' arguments are not found persuasive.

The credibility of the claimed invention is not at issue. Instead, it is the examiner's position that the claimed invention has no specific and substantial asserted utility and has no well-established utility, even after full consideration of the alleged "objective evidence" as provided in the specification. Each of these arguments will be described in more detail below. It should be noted that, contrary to appellants' assertion, the examiner has fully considered all evidence of record in evaluating the claims for utility under 35 USC § 101.

Appellants argue the claimed invention has specific, substantial, real-world utility as allegedly being useful for toxicology testing, drug discovery, and disease diagnosis through gene expression profiling. Appellants argue these uses are explained in the Bedilion and Furness Declarations, the substance of which is allegedly not rebutted by the examiner. Appellants argue there is no dispute that the claimed invention is a useful tool in cDNA microarrays used to perform gene expression analysis and in 2-D PAGE

and western blots to monitor protein expression and assess drug toxicity. Appellants assert that these uses are sufficient to establish utility for the claimed polynucleotide. Appellants' arguments are not found persuasive.

Regarding the substance of the Bedilion and Furness Declarations, the examiner agrees with the Bedilion and Furness Declarations to the extent that any polynucleotide can be included as part of a cDNA microarray and any polypeptide can be included as part of a 2-D PAGE and western blot, however, this does not confer patentable utility on the claimed compounds as these utilities are considered general uses and not utilities that are specific to the claimed invention. MPEP 2107.01 states, "A 'specific utility' is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention" (emphasis in original). Polynucleotides have a variety of general uses, such as for hybridization, protein expression, and as a component of a cDNA microarray – these uses are applicable to any polynucleotide and are not specific to the claimed polynucleotide. Similarly, polypeptides have a variety of general uses, such as for molecular weight markers and as components of 2-D PAGE and western blot – these uses apply to the general class of polypeptides. Also, the claimed compounds have no substantial utility. MPEP 2107.01 states, "Utilities that require or constitute carrying out further research to identify or reasonably confirm a 'real world' context of use are not substantial utilities". Since the specification does not disclose a correlation between any specific disease or disorder and an altered level or form of the claimed sequences and/or or guidance to allow a skilled artisan to interpret and use the results of expression monitoring, such results would be meaningless

without further research. MPEP 2107.01, citing an example of a utility that is not substantial, states, "[a] method of assaying for or identifying a material that itself has no specific and/or substantial utility". As the claimed compounds themselves have no specific and substantial utility, the use of the claimed compounds for expression monitoring to measure their expression levels is not substantial.

Appellants refer to the Bedilion declaration as explaining the many reasons why a person skilled in the art reading the Yue '566 application (provisional application to which the instant application claims benefit under 35 USC 119(e)) would have understood this application to disclose the claimed polynucleotide to be useful for a number of gene expression monitoring applications, such as a probe for expression of the polynucleotide in connection with the development of drugs and the monitoring of the activity of such drugs. Specifically, appellants quote from the Bedilion declaration stating that a cDNA microarray comprising the SEQ ID NO:12-encoding polynucleotide is more useful than a cDNA micrroarray without in connection with gene expression monitoring studies on drugs for the treatment of cancer, immune disorders, neurological disorders, and gastrointestinal disorders. Appellants' arguments are not found persuasive.

There is no evidence of record of a correlation between the claimed compounds and any disease state, including cancer, immune disorders, neurological disorders, and gastrointestinal disorders and, as such, the results of gene expression monitoring assays using a cDNA microarray comprising the claimed polynucleotide would be meaningless and any information obtained from an expression profile would only serve

as the basis for further experimentation on the observation itself. MPEP 2107.01 provides an example of a substantial utility as follows: "An assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would also define a 'real world' context of use". As stated above, the specification does not disclose a correlation between any specific disease or disorder and an altered level or form of the claimed polynucleotide. The specification does not disclose any results that would enable a skilled artisan to draw any conclusions regarding a disorder, namely, that the expression of the claimed polynucleotide is expressed at an altered level or form as compared to the corresponding normal tissue. Many genes expressed in diseased tissues have no connection to the disease itself and are not targets for drug development or toxicology.

Appellants discuss the Bedilion Declaration's detailed explanations of how cDNA technology can be used to conduct gene expression monitoring evaluations. Appellants point to Dr. Bedilion's pages of text and numerous subparts explaining the importance of this technology. Appellants cite Dr. Bedilion's explanation that those skilled in the art at the time of the invention would have appreciated the criticality of toxicity testing and how the teachings of the Yue '566 application include using gene expression analyses in toxicology testing. Appellants assert the Bedilion Declaration establishes that persons skilled in the art, guided by the instant specification, at the time of the invention, would have wanted their cDNA microarrays to comprise the claimed polynucleotide, because a microarray comprising the claimed polynucleotide would allegedly provide more useful results in gene expression monitoring studies than microarrays lacking the claimed

polynucleotide. Appellants argue that Dr. Bedilion's opinion by itself provides more than sufficient reason to compel the conclusion to persons skilled in the art that the claimed polynucleotide has a substantial, specific, and credible utility. Appellants' arguments are not found persuasive.

While there is no dispute that cDNA microarray technology is an extremely valuable technique in gene expression monitoring, toxicology testing, and drug efficacy testing, the claims are not drawn to this technique. Instead, the claims are directed to compounds that have no specific and substantial asserted utility. The specification fails to disclose a correlation of the claimed sequences with any particular disease or disorder and the specification provides no guidance as to how to interpret data obtained from gene expression analysis in toxicology testing. As stated above, any polynucleotide can be a component of a cDNA microarray and there is no evidence of record that would indicate that incorporating the claimed polynucleotide into a microarray would not make that microarray any more valuable than adding any other human polynucleotide. Thus, this asserted utility is not specific. Moreover, this asserted utility is not substantial as determining the relationship between the claimed polynucleotides and any specific disease or disorder or interpreting the results of gene expression monitoring based on the teachings of the instant specification would require further research to identify a "real world" context of use.

At the top of page 12 of the appeal brief, appellants argue the examiner does not address the "fact" that the claimed polynucleotide can be used as highly specific probes to measure both the existence and amount of complementary mRNA sequences known

to be expression products of the claimed polynucleotides. Appellants conclude that the claimed invention is not, in that regard, some random sequence whose value as a probe is speculative or would require further research to determine. Appellants' arguments are not found persuasive.

As stated above, any polynucleotide is a highly specific probe for itself or its complement, or any mRNA that can be transcribed from it. Such can be said for *any* polynucleotide. As previously stated, MPEP 2107.01 provides an example of a utility that is *not* substantial as follows: "A method of assaying for or identifying a material that itself has no specific and/or substantial utility". The claimed polynucleotide has no specific and/or substantial utility, therefore, the use of a cDNA microarray comprising the claimed polynucleotide for measuring levels of itself is *not* substantial.

Appellants argue the examiner does not address the alleged "fact" that the claimed polynucleotide can be used as a highly specific probe to measure both the existence and amount of complementary mRNA sequences known to be expression products of the claimed polynucleotides. Appellants conclude that the claimed invention is not, in that regard, some random sequence whose value as a probe is speculative or would require further research to determine. Appellants' arguments are not found persuasive.

As stated above, any polynucleotide is a highly specific probe for itself. Such can be said for any polynucleotide. MPEP 2107.01 makes clear that a method for assaying or identifying a material, in this case a nucleic acid, has no specific and/or substantial utility.

Appellants argue that, given that the claimed polynucleotide is known to be expressed, its utility as a measuring and analyzing instrument for expression levels is as indisputable as a scale's utility for measuring weight (citing Raytheon v Roper (supra) and In re Cortwright (supra)). Appellants' arguments are not found persuasive.

It is true that a scale, a gas chromatograph, screening assays, and nucleotide sequencing techniques have utility as research tools. However, such tools generate a result that requires no further experimentation for interpretation, e.g., a scale indicates the weight of an object and requires no further experimentation for interpretation of the result. In the instant case, a more representative analogy to the claimed polynucleotide and array would be that of a scale without an identifiable unit of measure - one could place an object on the scale, however, further research would be required to interpret the result and determine the weight of the object. Similarly, as there is no evidence of record of an association of the claimed polynucleotide with a disease state and the specification fails to provde guidance for interpreting the results of gene expression analysis, additional experimentation would be required to determine which – if any – disease is associated with the claimed polynucleotide and/or to interpret a result of altered polynucleotide expression obtained using a microarray comprising the claimed polynucleotide. Thus, the assertion that the claimed polynucleotide has patentable utility as a probe in, or a member of, a microarray is not substantial.

Appellants argue there can be no reasonable dispute that persons skilled in the art have numerous uses for information about relative gene expression including understanding the effects of a potential drug for treating cancer, immune disorders,

neurological disorders, and gastrointestinal disorders. Appellants argue that, since the specification discloses the claimed polynucleotide to be expressed in reproductive, gastrointestinal, and nervous system tissues and tissues associated with cancer and inflammation, there can be no dispute that an ordinarily skilled artisan could put the claimed invention to such use, e.g., to derive more information about relative gene expression than without it. Appellants' arguments are not found persuasive.

While the specification does indicate that the nucleic acid of SEQ ID NO:64 is expressed in reproductive, gastrointestinal, and nervous system tissues (page 91 of the specification), there is no indication that expression of SEQ ID NO:64 is exclusively in reproductive, gastrointestinal, and nervous system tissues and there is no indication that SEQ ID NO:64 is expressed exclusively in diseased tissues as opposed to normal tissues. The specification does not disclose the claimed polynucleotide as being expressed at an altered level or form in any particular disease or disorder as compared to the corresponding normal tissue(s). Furthermore, even if it can be assumed arguendo that the claimed polynucleotide plays a role in the myriad of disclosed disorders, determining which disorder(s) is/are involved and if and how the claimed polynucleotide is associated with the disorder would require further research to identify a "real world" use.

Appellants refer to Dr. Bedilion's opinionated discussion of Brown et al. (US Patent 5,807,522, cited by appellants). Dr. Bedilion characterizes the patent as providing evidence that microarrays can be used in numerous genetic applications, including monitoring of gene expression in different tissue types, disease states, in

response to drugs, and in response to potential toxins. Appellants cite the references of Rockett et al. (Xenobiotica 29:655) and Lashkari et al. (PNAS 94:8945) as allegedly describing the use and importance of gene expression technology with respect to drug screening and toxicology testing. Appellants' arguments are not found persuasive.

It is noted that the claims of the Brown et al. patent are drawn to methods of forming microarrays (see, for example, claim 1 of Brown et al.). However, in the instant case, the claims are drawn to a microarray comprising the claimed polynucleotide, which does not have patentable utility as stated in detail above. Appellants' arguments and alleged supporting evidence merely indicate that microarray technology is important and useful to the scientific community. These publications are silent with respect to the claimed polynucleotide and fail to demonstrate the claimed invention has any patentable utility. It is the examiner's position that this asserted utility for the claimed polynucleotide is not specific and due to the lack of guidance provided by the specification, the asserted utility is not substantial.

Appellants assert that the Furness Declaration explains reasons why a skilled artisan, reading the Yue '566 application, would have understood the application to disclose the claimed polypeptide to be useful for gene and protein expression monitoring in connection with the development of drugs and monitoring the activity of such drugs using in particular 2-D PAGE. Appellants argue the claimed invention makes 2-D PAGE a more powerful tool for toxicology testing and drug efficacy testing as allegedly more information can be derived with the claimed invention than without it. Appellants argue that the opinions of the Furness Declaration are confirmed in the

literature prior to the filing of the instant application. Appellants' argument is not found persuasive.

As with gene expression monitoring, there is no dispute that 2-D PAGE analysis is an extremely valuable technique. However, the claims are not drawn to this technique. Instead, the claims are directed to a polynucleotide, a polypeptide, and an array that have no specific and substantial asserted utility. The examiner agrees that, along with any other protein, SEQ ID NO:12 can be used in 2-D PAGE gels and western blots in drug toxicity monitoring – this non-specific use applies to the broad class of proteins. Furthermore, the specification provides no guidance to allow a skilled artisan to use data relating to the claimed polypeptide derived from the results of toxicity testing and what the results would mean. For example, if the expression of the claimed polypeptide were monitored in a drug toxicity test, the specification provides no basis on which a skilled worker would be able to determine whether that result is meaningful. As such, further experimentation would be required to interpret the results of such 2-D PAGE analysis.

At the top of page 15 of the appeal brief, appellants argue the claimed sequences are useful as tools for toxicology testing, drug discovery, and the diagnosis of disease and that these uses are "well-established". Appellants cite the references of Rockett et al. (Xenobiotica 29:655), Nuwaysir et al. (Mol Carcinogen 153:24), Steiner et al. (Toxicol Lett 467 :112-113), and Rockett et al. (Environ Health Perspectives 107:681) and an email from Dr. Cynthia Afshari to an Incyte employee, and further cite examples (page 16, bottom of the appeal brief) that allegedly support appellants'

assertions. Appellants assert that "there is no expressed gene which is irrelevant to screening for toxicological effects, and all expressed genes have a utility for toxicological screening".

Appellants state, "[t]he instant application claims priority to United States Provisional Application Serial No. 60/139,566 filed June 16, 1999" (page 9, middle of the appeal brief). It should be noted that appellants' reliance on the references of Rocket et al. (Xenobiotica 7:655), Nuwaysir et al. (Mol Carcinogen 153:24), Steiner et al. (Toxicol Lett 467 :112-113), and Rockett et al. (Environ Health Perspectives 107:681) is improper as these references were NOT available to one of ordinary skill in the art at the time of the invention. MPEP 2164.05(a) makes clear that the specification must be enabling as of the filing date of the application and, while MPEP 2164.05(a) states, "The specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known to those skilled and already available to the public," it is noted that the teachings of Gerke et al. (supra) and Nguyen et al. (supra) were not available to the public at the time of the invention.

Regarding the merit of appellants' argument, each of these uses (toxicology testing, drug development, and disease diagnosis) will be addressed individually, because the facts and issues directed to each use are distinct and separable. First, appellants argue that toxicology testing is a well-established utility and that the claimed invention therefore possesses patentable utility. However, for a utility to be "well-established" it must be specific, substantial and credible. In this case, such a use would apply to the broad class of expressed polynucleotides as acknowledged by appellant

("all expressed genes have a utility for toxicology testing" page 16 of the appeal brief). Therefore, this use is not specific. Furthermore, the specification fails to provide guidance regarding the significance and interpretation of the results of toxicology testing using the claimed compounds and none is known in the prior art. Therefore, further experimentation would be required to identify a "real world" use for the claimed compounds. As such, this asserted utility is neither specific and substantial nor well-established.

With regard to drug discovery and development, appellants cite expression profiling as one use for the claimed compounds. Appellants refer to recent developments as providing evidence that the benefits of this information are already beginning to manifest themselves. However, appellants are incorrect in asserting that the efficacy (ability to produce a desired effect) of a compound could be evaluated from the result of a transcript image because there is no way to assess the meaning of any individual "hit" obtained from this procedure. The first requirement is that one must know the biological significance of the compound(s) that is/are being evaluated. Without this information, the results of the transcript image are useless because one would not inherently recognize how to interpret the result of increased or decreased polynucleotide or protein expression or even what significance could be attributed to such changes in expression profiles. As this information has not been provided in the specification, further experimentation is required to identify a "real world" use for the claimed polynucleotide.

With regard to diagnosis of disease, in order for a polynucleotide or polypeptide to be so useful for diagnosis of a disease, there must be a "well-established" or disclosed correlation or relationship between the claimed compounds and a disease or disorder. The presence of a polynucleotide in tissue that is derived from diseased tissues is not sufficient for establishing a utility in diagnosis of disease in the absence of some information regarding a correlative or causal relationship between the expression of the claimed polynucleotide or polypeptide and the disease. If a molecule is to be used as a surrogate for a disease state, some disease state must be associated in some way with the molecule. There must be some expression pattern that would allow the claimed compounds to be used in a diagnostic manner. Many polynucleotides and their encoded polypeptides are expressed at equal levels and in identical forms in both normal *and* diseased tissues. Evidence of a differential expression may serve as a basis for use of the claimed compounds as a diagnostic for disease(s). However, in the absence of any disclosed relationship between the claimed polynucleotides or encoded proteins and any disease or disorder and the lack of any correlation between the claimed polynucleotides or the encoded proteins with any known disease or disorder, any information obtained from an expression profile would only serve as the basis for further research on the observation itself. Also, because any potential diagnostic utility is not yet known and has not yet been disclosed, the utility is not substantial because it is not currently available in practical form and would thus require further research for its implementation.

Appellants argue that there is a substantial likelihood that the claimed INTRA-12 is functionally related to annexin 31 and pemphaxin, polypeptides of alleged undisputed utility. Appellants argue that there is by implication a substantial likelihood that the claimed compounds are similarly useful and that appellants need not show more to demonstrate utility (citing *In re Brana*, 51 F3d 1560, 1566; 34 USPQ2d 1436 (Fed Cir 1995)). Appellants argue that the claimed polypeptide shares amino acid sequence identity with annexin 31 and pemphaxin, proteins that have been implicated in various diseases and that this evidence corroborates appellants assertion that the claimed compounds may be useful in the diagnosis and treatment of autoimmune disorders. Appellants' argument is not found persuasive.

Appellants state, "[t]he instant application claims priority to United States Provisional Application Serial No. 60/139,566 filed June 16, 1999" (page 9, middle of the appeal brief). It should be noted that appellants' reliance on the references of Gerke et al. (Physiol Rev 82 :331-371) and Nguyen et al. (J Biol Chem 275:29466-29476) as allegedly providing evidence that annexin 31 and pemphaxin are involved in disease states is improper as these references were NOT available to one of ordinary skill in the art at the time of the invention. MPEP 2164.05(a) makes clear that the specification must be enabling as of the filing date of the application and, while MPEP 2164.05(a) states, "The specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known to those skilled and already available to the public," it is noted that the teachings of Gerke et al. (supra) and Nguyen et al. (supra) were not available to the public at the time of the invention.

Regarding the merit of appellants' argument, it is noted that in Brana, the claimed invention was shown to have patentable utility based on evidence provided in the specification demonstrating *in vitro* anticancer activity of the claimed compound, which was structurally related to similar compounds that were proven chemotherapeutic agents. In contrast to Brana, there is no evidence of record that would indicate that the claimed polypeptide has annexin biological activity, and even assuming such were the case, there is no well-established utility for the annexin class of polypeptides or, more specifically, annexin 31 and pemphaxin. It should be noted that the specification fails to disclose that SEQ ID NO:12 shares amino acid sequence identity with pemphaxin. Instead, the specification identifies only annexin 31 as a "homologous" sequence (see page 80 of the specification). Regardless, there is no dispute that the claimed polypeptide shares amino acid sequence identity with annexin 31 and pemphaxin. However, this is no indication that the claimed polypeptide has annexin 31 or pemphaxin biological activity. It is just as likely that that the claimed polypeptide is a non-functional mutant of annexin 31 or pemphaxin. Even if SEQ ID NO:12 had biological activity equivalent to annexin 31 or pemphaxin, it is not clear from the prior art that annexin 31 and pemphaxin have any specific utility that can be imputed to the claimed polynucleotide or polypeptide. While the homology between the sequence of SEQ ID NO:12 and annexin 31 or pemphaxin is sufficient to believe that they may have the same utility, it is not clear what utility the proteins have.

It should also be noted that it is unclear to the examiner as to how SEQ ID NO:12, which is structurally distinct from pemphaxin can – at the same time – be

pemphaxin. While two compounds may be structurally similar, this does not make them identical, as asserted by appellants. In this case, because SEQ ID NO:12 is structurally distinct from pemphaxin, SEQ ID NO:12 cannot be pemphaxin and has not been recognized as such. Even assuming SEQ ID NO:12 were pemphaxin – which it is not – the specification provides no guidance for using SEQ ID NO:12 for diagnosing or treating an autoimmune disorder. Thus, further experimentation would be required to determine which – if any – autoimmune disorder(s) SEQ ID NO:12 is/are so useful in diagnosing and treating and if SEQ ID NO:12 is so useful, how to use SEQ ID NO:12 for diagnosing and treating an autoimmune disorder or disorders.

Appellants argue that members of the annexin class of proteins have been used as cell markers due to their phospholipid binding properties and their association with the plasma membrane, citing the use of radiolabeled Annexin V in radionuclide imaging. Appellants argue that radionuclide imaging using radiolabeled annexins may be useful for disease diagnosis. Appellants argue that such use is independent of the presence of calcium binding sites, citing the examples of annexin I, annexin II, annexin A11, and annexin XIII. Appellants argue that SEQ ID NO:12 is more likely than not a phospholipid-binding protein and is useful like other annexin family members. Appellants argue the examiner must accept appellants' assertion that the claimed polypeptide is pemphaxin and thus has its utility unless the examiner can demonstrate otherwise, which is allegedly not the case. Appellants' argument is not found persuasive.

Appellants state, "[t]he instant application claims priority to United States Provisional Application Serial No. 60/139,566 filed June 16, 1999" (page 9, middle of the appeal brief). It should be noted that appellants' reliance on the references of Blankenberg et al. (Eur J Nucl Med 27:359-367), Lecona et al. (Biochem J 373:437-449), and Lecat et al. (J Cell Sci 113:2607-2618) as allegedly providing evidence that annexin V can be used in radionuclide imaging and that annexins can associate with membranes in the absence of calcium is improper as these references were NOT available to one of ordinary skill in the art at the time of the invention. MPEP 2164.05(a) makes clear that the specification must be enabling as of the filing date of the application and, while MPEP 2164.05(a) states, "The specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known to those skilled and already available to the public," it is noted that the teachings of Blankenberg et al. (supra), Lecona et al. (supra), and Lecat et al. (supra) were not available to the public at the time of the invention.

Regarding the merit of appellants' argument, it is noted that there is no evidence of record, including appellants' cited references, that the sequence disclosed in the specification as being "homologous" to SEQ ID NO:12, i.e., annexin 31, can be used for radionuclide imaging or as a cell marker, and based on the prior art, one would not expect annexin 31 to be so useful. For example, Morgan et al. (supra) teach "[t]ype II calcium-binding sites... ...have been identified as the principal mechanism by which annexins.....bind phospholipids... ...to perform various membrane-related functions" (page 300, left column, top) and that annexin 31 was found to have "a complete ablation

of all four type II calcium-binding sites" (page 300, abstract). Morgan et al. are silent as to whether annexin 31 has the ability to bind phospholipid in the absence of calcium and there is no evidence of record that such a property can be determined a priori, and thus further research would be required to determine if annexin 31 has the ability to bind phospholipid in the absence of calcium. Even if annexin 31 has this characteristic, it is noted that there is no evidence of record to indicate that SEQ ID NO:12 has annexin biological activity, particularly phospholipid binding activity and it is just as likely that SEQ ID NO:12 is a non-functional mutant of annexin 31. In the absence of such evidence, appellants have failed to demonstrate that SEQ ID NO:12 has such utility and further experimentation would be required to determine if SEQ ID NO:12 can be used for radionuclide imaging and/or as a cell marker. Even assuming arguendo the specification demonstrated and asserted phospholipid binding activity of SEQ ID NO:12, the specification provides no guidance for using SEQ ID NO:12 for radionuclide imaging or as a cell marker, thus requiring further experimentation for such use. As stated above, the specification fails to disclose that SEQ ID NO:12 shares amino acid sequence identity with pemphaxin and it is unclear to the examiner as to how SEQ ID NO:12, which is structurally distinct from pemphaxin can – at the same time – be pemphaxin. While two compounds may be structurally similar, this does not make them identical. In this case, because SEQ ID NO:12 is structurally distinct from pemphaxin, SEQ ID NO:12 cannot be pemphaxin and has not been recognized as such. In this case, it is just as likely that SEQ ID NO:12 is a non-functional mutant of pemphaxin. Even assuming SEQ ID NO:12 were pemphaxin – which it is not – there is no evidence

of record that pemphaxin is useful for radionuclide imaging or as a cell marker and further research would be required to determine if SEQ ID NO:12 can be used for radionuclide imaging and/or as a cell marker. Thus, it is not clear from the prior art that either all annexins or specifically annexin 31 and pemphaxin have any specific utility that can be imputed to the claimed polynucleotide or polypeptide. While the homology between the sequence of SEQ ID NO:12 and annexin 31 or pemphaxin is sufficient to believe that they may have the same utility, it is not clear what utility the proteins have.

Appellants argue that none of the examiner's cited references disputes functional assignment by a reasonable probability, citing Brenner's basic "rule". Appellants argue that at most the cited references indicate that it is difficult to make functional assignments with certainty and that this is not the required standard. Appellants argue that the teachings of Seffernick et al. do not contradict the findings of Brenner et al. Appellants' argument is not found persuasive.

There is no dispute that one can predict function based on similarities between two or more amino acid sequences. However, in this case, appellants attempt to use the similarities between two amino acid sequences as absolute proof that: 1) a polypeptide is biologically active and 2) has the same function as the homologous sequence. This is clearly not the intent of functional prediction, which only provides a starting point for empirical research to identify a polypeptide's true function. Appellants fail to address the fact that, while function can be predicted, it cannot be demonstrated by functional assignment and, in this case, it is just as likely that SEQ ID NO:12 is a non-functional mutant – there is simply no way to know based on functional assignment alone. As to

Brenner's "rule" (although not expressly stated, it appears appellants are referring to the reference of Brenner et al. PNAS 95:6073-6078), it is noted that appellants attempt to use teachings that clearly are not relevant to SEQ ID NO:12 to support their argument. Nowhere does the reference of Brenner et al. (supra) suggest that the disclosed results can be extrapolated for use in predicting functional homology of any protein. Moreover, one of skill in the art would recognize that such teachings do not apply to other proteins as Brenner et al. (supra) teach their comparisons "have been assessed using proteins whose relationships are known reliably from their structures and functions, as described in the SCOP database" (page 6073, abstract). The art recognizes the proteins within the SCOP database have been fully characterized, meaning their functions have been characterized by empirical laboratory experiments and their three dimensional structures have been generated (see Murzin et al. J Mol Biol 247:536-540). Brenner et al. (supra) are silent as to the use of their results to the functional assignment of an uncharacterized protein. In this case, appellants use a portion of the text of Brenner et al. (supra) out of context and attempt to use these teachings to inappropriately support their argument. One of skill in the art reading Brenner et al. (supra) would recognize that the disclosed teachings are applicable ONLY for identifying evolutionary homology – not functional homology. Even assuming *arguendo* that the results of Brenner et al. (supra) could be applied to functional annotation – which they cannot – it is unclear as to whether these results would be applicable to an uncharacterized protein as Brenner et al. (supra) teach their results are specific for the database used in the study by stating that their result is "a reliable threshold for [the PDB90D-B database]" and that their

findings are for "a database of this particular size and composition". In the instant case, neither the specification nor the prior art provides a functional characterization of SEQ ID NO:12 and there is no evidence of record that SEQ ID NO:12 is biologically active and it is just as likely that SEQ ID NO:12 has no function at all. Brenner, who, in a separate reference (Brenner Trends Genet 15:132-133) describing the erroneous use of functional assignment, clearly indicates that empirical evidence – not prediction – is required to demonstrate function.

Appellants argue the examiner has not provided evidence that any member of the annexin family is not useful and that the only reasonable inference is that SEQ ID NO:12 must be useful. Appellants' argument is not found persuasive.

The specification discloses that the amino acid sequence of SEQ ID NO:12 is "homologous" to annexin 31 (citing the reference of Morgan et al. supra). Morgan et al. (supra) provide evidence that at least the sequence disclosed to be "homologous" to SEQ ID NO:12 is useful only for further research. Addressing annexins in general, Morgan et al. teach that there is a lack of understanding of the biological significance of annexins by stating, "[t]he biological function(s) and phenotypic profile(s) of annexins remain unresolved" (page 300, left column, top). Furthermore, Morgan et al. teach that annexin 31 has a distinct expression pattern, an amino acid sequence that is atypical of annexin family members, and has no calcium binding sites and thus "constitutes a unique, natural probe for investigating the role of membrane binding in annexin function" and that the "discovery of human annexin 31 adds a new dimension to annexin research (page 300, abstract and page 303, Discussion).

Beginning at the top of page 20 of the appeal brief, appellants argue that a "real-world" utility exists if actual use or commercial success can be shown and that a showing of actual use or commercial success is conclusive proof of utility. Appellants argue that a vibrant market has developed for databases containing all expressed genes, including those of Incyte, the real party at interest. Appellants state Incyte's customers and the scientific community have acknowledged that Incyte's databases have proven valuable, and that the databases including the claimed polynucleotide would be even more valuable. Appellants argue that customers can purchase the claimed polynucleotides from Incyte, saving the customer time and expense. Appellants' arguments are not found persuasive.

A rejection under 35 U.S.C. § 101 for lack of operability can be overcome by a showing of actual use or commercial success. The instant issue is whether or not the asserted utilities are substantial and specific. Such is not necessarily addressed by a showing of commercial success or actual use. Many products that lack patentable utility, e.g., a pet rock, enjoy commercial success, are used, and are considered valuable. Furthermore, there is no evidence to suggest that a database is any more or less valuable with the inclusion of the claimed compounds or that customers would desire to purchase the claimed compounds.

Appellants argue that rather than responding to the evidence allegedly demonstrating utility, the examiner attempts to dismiss it altogether by arguing that the disclosed and well-established utilities for the clamed polynucleotides are not "specific

and substantial asserted" utilities. Appellants argue the examiner is incorrect both as a matter of law and as a matter of fact. Appellants' arguments are not found persuasive.

The claimed invention has no well-established use and there is no specific and substantial use for the claimed invention, even after FULL consideration of the "evidence" as provided in the specification. Appellants' arguments will be addressed in detail below.

Appellants characterize the examiner's rejection as being based on the grounds that, without information as to the precise biological role of the claimed invention, the claimed invention lacks specific patentable utility. Appellants argue that, according to the examiner, it is not enough that a person skilled in the art could use and would want to use the claimed invention either by itself or in a microarray, a 2-D PAGE, or a western blot for expression analysis, but that appellants are also required to provide a specific and substantial interpretation of the results generated in a given expression analysis. Appellants argue that specific and substantial interpretations regarding biological function may be required by technical journals, but are not necessary for patents. Appellants state the relevant question is not how or why the invention works, but whether the invention provides an identifiable benefit in currently available form. Appellants argue that the present invention meets this test. Appellants argue that the threshold for patentable utility is low and that only throwaway utilities are insufficient, and that knowledge of biological function is not required. Appellants' arguments are not found persuasive.

It is noted that appellants' arguments have mischaracterized the examiner's position. The examiner has fully considered appellants' "evidence" allegedly demonstrating utility and, in accordance with 35 USC § 101 has determined the claimed invention to lack patentable utility. The examiner acknowledges that biological function of the claimed compounds is not necessarily required for patentable utility – only that the claimed invention have a specific, substantial, and credible utility or a well-established utility. In this case, the rejection never states that the precise biological role of a polynucleotide is required for it to possess patentable utility. The examiner provides the example of Shattuck-Eidens et al. (US Patent 5,693,473), who teach mutant alleles of the *BRCA1* gene that predispose a patient to developing breast and ovarian cancers (abstract). While there is no disclosure of the function of the mutant *BRCA1* genes or their gene products, the invention nevertheless has utility as being an indicator for susceptibility to developing breast and ovarian cancers. Contrary to this example, the specification fails to disclose sufficient information such that one of skill in the art can use the claimed compounds as a disease marker or for toxicology testing, drug discovery, or disease diagnosis and as such, there is no specific and substantial asserted utility. For example, if the claimed polynucleotide were used in a microarray for toxicology testing and if a compound caused the claimed polynucleotide to be expressed at a decreased level as demonstrated by the data generated using the microarray, what information does this provide, other than to initiate further experimentation to interpret the result? In view of the specification, a skilled artisan would recognize that this determination requires further research, and thus the asserted

utility is not substantial. It should also be noted that any expressed polynucleotide can be used in a microarray and any polypeptide can be used for 2-D PAGE and western blotting and thus the asserted utilities are not specific.

Beginning at the middle of page 22 of the appeal brief, appellants argue that despite the evidence that SEQ ID NO:12 is related to pemphaxin, the examiner has refused to impute the utility of pemphaxin to INTRA-12 (SEQ ID NO:12). Appellants argue the examiner takes the position that utility of the claimed compounds cannot be imputed unless appellants identify which particular annexin function is possessed by INTRA-12. Appellants argue the examiner would require that all annexins possess a "common" utility in order to demonstrate utility by membership in a class. Appellants state the case law requires only that the class not contain a substantial number of useless members. Appellants argue the examiner has treated INTRA-12 as if it was in a general class of all polynucleotides and polypeptides, rather than the annexin class. Appellants argue the examiner has not presented any evidence that the annexin class of proteins has any, let alone a substantial number, of useless members. Appellants argue that even if the examiner's common utility criterion were correct, the annexin family would meet it. Appellants argue annexin family members function in phospholipid binding, membrane-cytoskeleton interactions, phospholipase inhbition, anticoagulation, and membrane fusion, and the person of ordinary skill in the art need not know anything more about the claimed invention in order to be able to use it and the Office action presents no evidence to the contrary. Appellants argue the examiner concludes that a skilled artisan would need to know whether any given annexin functions in phospholipid

binding, membrane-cytoskeleton interactions, phospholipase inhbition and that INTRA-12 is useful only for further study of INTRA-12. Appellants argue that knowledge that INTRA-12 is an annexin related to annexin 31 is sufficient to make it useful for diagnosis and treatment of cancer, immune disorders, neurological disorders, and gastrointestinal disorders. Appellants conclude that these facts must be accepted as true in the absence of evidence or sound scientific reasoning to the contrary. Appellants' argument is not found persuasive.

It should be noted that the specification fails to teach that the claimed polypeptide is related to pemphaxin and instead only discloses that the sequence of SEQ ID NO:12 is "homologous" to annexin 31 (page 80). Appellants' reliance on the reference of Nguyen et al. (J Biol Chem 275:29466-29476) as allegedly providing evidence that SEQ ID NO:12 is related to pemphaxin is improper as this references was NOT available to one of ordinary skill in the art at the time of the invention. MPEP 2164.05(a) makes clear that the specification must be enabling as of the filing date of the application and, while MPEP 2164.05(a) states, "The specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known to those skilled and already available to the public," it is noted that the teachings of Nguyen et al. (supra) were not available to the public at the time of the invention. Furthermore, as stated above, although SEQ ID NO:12 may be related to a member of the annexin family, i.e., annexin 31 as disclosed by Morgan et al. (supra), by sequence, there is no evidence of record that it is related by function. The specification merely indicates that the amino acid sequence of SEQ ID NO:12 is "homologous" to annexin 31 of Morgan et al.

(supra), who teach that the biological significance of annexins is unresolved and that annexin 31 is useful only for further research based on its structurally and functionally distinct properties as compared to other annexin polypeptides. Morgan et al. (supra) fail to provide evidence that annexin 31 functions in phospholipid binding, membrane-cytoskeleton interactions, phospholipase inhbition, anticoagulation, and membrane fusion and/or have the ability to diagnose and treat cancer, immune disorders, neurological disorders, and gastrointestinal disorders. Moreover, the specification fails to provide evidence and the necessary guidance for using SEQ ID NO:12 for phospholipid binding, membrane-cytoskeleton interactions, phospholipase inhbition, anticoagulation, and membrane fusion and diagnosing and treating cancer, immune disorders, neurological disorders, and gastrointestinal disorders. Thus, it is not clear from the prior art and the specification that either all annexins or specifically annexin 31 or pemphaxin have any specific utility that can be imputed to the claimed polynucleotide or polypeptide. While the homology between the sequence of SEQ ID NO:12 and annexin 31 or pemphaxin is sufficient to believe that they would have the same utility, it is not clear what utility both proteins have.

At the top of page 24 of the appeal brief, appellants argue the rejection is incorrectly based on the grounds that the use of an invention as a tool for research is not a substantial use. Appellants state that only a limited subset of research uses are not substantial: those in which the only known use for the claimed invention is to be an object of further study, thus merely inviting further research. Appellants argue that nowhere in the cited case law is it stated or implied that a material cannot be patentable

if it has some other, additional beneficial use in research. Appellants' arguments are not found persuasive.

As discussed above, whereas a scale or gas chromatograph has patentable utility as a research tool as providing a result that can be readily used and provides a specific benefit in currently available form. Also, DNA ligases have a well-established utility. In contrast to these examples, the claimed compounds do NOT provide a specific benefit in currently available form, the claimed compounds have no well-established utility, and use of the claimed compounds would require further experimentation to identify a "real world" use. The claimed compounds are not disclosed as having a property that can be identifiably and specifically useful without further experimentation. The claimed invention is, in fact, the object of further study, merely inviting further research – as evidenced at least by Morgan et al. (supra). None of the asserted utilities for the claimed compounds is specific and substantial and/or well-established.

At the top of page 24 of the appeal brief, appellants argue the claimed invention has a beneficial use and that the claimed compounds are tools not an object of research. Appellants argue the data generated as a result of gene expression monitoring using the claimed invention is not merely to study the polynucleotide itself, but to study properties of tissues, cells, and potential drug candidates and toxins. Appellants argue that without the claimed invention, information regarding properties of tissues, cells, and potential drug candidates and toxins is less complete. Appellants argue SEQ ID NO:12 shares homology with other annexin family members and that one allegedly would have considered INTRA to be a valuable tool for use in research on

cancer, immune disorders, neurological disorders, and gastrointestinal disorders. Appellants argue the claimed invention has numerous other uses as a research tool, each of which is substantial, such as diagnostic assays, chromosomal markers, and ligand screening assays.

As previously stated, the specification fails to provide guidance regarding the interpretation of any results of expression monitoring using either the claimed polynucleotide or polypeptide and as such, further research is required to establish a "real-world" use for the claimed compounds. In regards to appellants' asserted use of the claimed polynucleotide for chromosomal mapping, it is noted that any human polynucleotide can be used for chromosomal mapping – this utility is not specific. Regarding appellants' asserted use of the claimed polynucleotide for diagnostic assays, in order for a polynucleotide to be useful, as asserted, for diagnostic assay, there must be a well-established or disclosed correlation or relationship between the claimed polynucleotide and a disease or disorder. The presence of a polynucleotide in a diseased tissue is not sufficient for establishing a utility in diagnosis of disease in the absence of some information regarding a correlative or causal relationship between the expression of the claimed polynucleotide and the disease. If a molecule is to be used as a surrogate for a disease state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed polynucleotide to be used in a diagnostic manner. Many polynucleotides are expressed at equal levels and in identical forms in both normal *and* diseased tissues. In the absence of any disclosed relationship between the claimed polynucleotides or encoded

proteins and any disease or disorder and the lack of any correlation between the claimed polynucleotides or the encoded proteins with any known disease or disorder, any information obtained from an expression profile would only serve as the basis for further research on the observation itself. Also, because any potential diagnostic utility is not yet known and has not yet been disclosed, the utility is not substantial because it is not currently available in practical form and would thus require further research for its implementation. Thus, the disclosure does not present a substantial utility that would support the requirement of 35 U.S.C. § 101. Regarding the asserted use of the claimed compounds for ligand screening assays, this utility is not specific as any polynucleotide or polypeptide can be used as a target to identify potential ligands.

Beginning at the bottom of page 25 of the appeal brief, appellants challenge the legality of the Patent Examination Utility Guidelines. Appellants argue that "unique" or "particular" utilities have never been required by the law and appellants are unaware of any court that has rejected an assertion of utility on the grounds that it is not "particular" or "unique" to the specific invention. Appellants argue that to meet the utility requirement, the invention need only by "practically useful" and confer a "specific benefit" on the public. Appellants' arguments are not found persuasive.

Regarding the Training Materials, appellants are reminded that the examiner must examine a patent application according to the guidelines set forth by the USPTO as well as the MPEP, since the examiner has no authority to disregard such guidelines or to apply his own interpretation of patent law in the examination of the application. Furthermore, as set forth in the guidelines and the MPEP, the guidelines were

promulgated by the Patent Office in accordance with all applicable case law and thus are believed to be consistent therewith. Appellants are further reminded that the examiner has no authority to comment in regard to the legality of the new utility guidelines or the MPEP as set forth by the USPTO. Accordingly, it is the examiner's position that the instant claims, based on an analysis of the utility requirement of 35 USC § 101 and following the current Utility Guidelines, have no specific, substantial, or credible utility.

Regarding appellants' comments regarding a "unique" utility, it is noted that appellants' characterization of the examiner's position is misplaced. The examiner has not required appellants to identify a utility that is unique, i.e., not shared by any other compounds or compositions. Rather, appellants have been required to identify a utility that is specific to the invention claimed, as opposed to one that would apply regardless of the specific properties of the claimed invention. An invention certainly can have a utility that is shared by other compounds or compositions. While a utility need not be unique to a claimed invention, it must nonetheless be specific, and in currently available form, in order to satisfy 35 USC § 101.

Rejection under 35 USC § 112, First Paragraph

Appellants traverse the instant rejection by arguing that to the extent the instant rejection is based on the alleged improper allegation of lack of patentable utility under 35 USC 101, it allegedly fails for the same reasons. Appellants' argument is not found persuasive.

It is the examiner's position that the claimed invention has no substantial and specific asserted utility or a well-established utility for those reasons as stated above (addressing the rejection under 35 USC 101) and reiterated herein.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

DAVID STEADMAN
PATENT EXAMINER

David J. Steadman
April 15, 2004

Conferees
Ponnathapura Achutamurthy
Supervisory Patent Examiner
Art Unit 1652

PONNATHAPU ACHUTAMURTHY
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Michael Wityshyn
Supervisory Patent Examiner
Art Unit 1651

Michael G. Wityshyn (CONFEREE)
Supervisory Patent Examiner
Technology Center 1600

INCYTE CORPORATION (formerly known as Incyte Genomics, Inc.)
3160 PORTER DRIVE
PALO ALTO, CA 94304